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Relationship between Optic Disc Hemorrhage and Glaucoma among patients diagnosed with Systemic Hypertension and Diabetes Mellitus: The Colombian Glaucoma Study

Carlos Eduardo Rivera ^{a,b,c,d,*}, Maria Catalina Ferreria ^{a,b,e}, Laura Libreros-Peña ^{a,b}, M. Ahsan Shah ^a, Juan Carlos Aristizabal ^{a,b}, Edgar Muñoz ^{a,f}, Catalina Gomez-Duarte ^b, Beatriz Eugenia Ossa-Lopez ^b, Gabriel Burbano-Montenegro ^b, Ankur Seth ^{a,c,d,e}

^a Collective Innovations, Cali, Colombia

^b Pontificia Universidad Javeriana, Cali, Colombia

^c McWilliams Collective, USA

^d GSR Medical Center, Cali, Colombia

^e University of Tennessee Health Science Center, Memphis, Tennessee, USA

^f University of Texas Health, San Antonio, Texas, USA

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ABSTRACT

Introduction: Glaucoma is a leading cause of irreversible blindness worldwide; several risk factors have been identified as major underlying causes for developing this condition. Optic disc hemorrhage has been identified as a risk factor for the development and progression of primary open-angle glaucoma, as well it has been related to playing an important role in normal-tension glaucoma.

Material and methods: A cross-sectional study was conducted in Colombia among hypertensive and diabetic patients. This study included 2,067 subjects older than 50 years who were attended by a group of ophthalmologists in six cities in Colombia who conducted a complete medical and ophthalmological examination and applied standardized questionnaires and interviews aiming to evaluate participant's health conditions and lifestyles.

Results: We found a prevalence of Optic disc hemorrhage (ODH) of 0.4%. ODH presented an OR: 8.82 (95% CI 1.60 - 48.52) for the presence of Glaucoma. Patients diagnosed with systemic hypertension had an OR: 0.02 (95% CI 0.00 - 0.96); Patients with Retinal Nerve Fiber Layer Defect (RNFL) presented an OR: 509.40 (95% CI 8.60 - 30152.97) for the presence of ODH and 50% of patients with ODH did not have a diagnosis of glaucoma.

Conclusions: Despite the low prevalence of ODH in our study (0.4%), its presence is a High-risk factor for the presence of Glaucoma. RNFL defect is also highly related to ODH and the presence of Glaucoma.

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* Corresponding author.

E-mail address: carlosrivera.collective@gmail.com

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Relación entre Hemorragia de Disco Óptico y Glaucoma en pacientes con diagnóstico de Hipertensión Sistémica y Diabetes Mellitus: Estudio Colombiano de Glaucoma

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RESUMEN

Introducción: El glaucoma es una de las principales causas de ceguera irreversible a nivel mundial; varios factores de riesgo han sido identificados como las principales causas subyacentes para el desarrollo de esta condición. La hemorragia del disco óptico se ha identificado como un factor de riesgo para el desarrollo y progresión del glaucoma primario de ángulo abierto, así como también se ha relacionado con desempeñar un papel importante en el glaucoma de tensión normal.

Material y métodos: Se realizó un estudio transversal en Colombia entre pacientes hipertensos y diabéticos. Este estudio incluyó a 2.067 sujetos mayores de 50 años que fueron atendidos por un grupo de oftalmólogos en seis ciudades de Colombia, quienes realizaron un examen médico y oftalmológico completo y aplicaron cuestionarios y entrevistas estandarizados con el fin de evaluar las condiciones de salud y estilos de vida de los participantes.

Resultados: Encontramos una prevalencia de hemorragia del disco óptico (HDO) del 0,4%. ODH presentó un OR: 8,82 (IC 95% 1,60 - 48,52) para la presencia de Glaucoma. Los pacientes diagnosticados de hipertensión sistémica tuvieron OR: 0,02 (IC 95% 0,00 - 0,96); Los pacientes con Defecto de la Capa de Fibras Nerviosas de la Retina (RNFL) presentaron un OR: 509,40 (IC 95% 8,60 - 30152,97) para la presencia de ODH y el 50% de los pacientes con ODH no tenían diagnóstico de glaucoma.

Conclusiones: A pesar de la baja prevalencia de HDO en nuestro estudio (0,4%), su presencia es un factor de alto riesgo para la presencia de Glaucoma. El defecto de la RNFL también está muy relacionado con la ODH y la presencia de glaucoma.

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1. INTRODUCTION

Glaucoma is a leading cause of irreversible blindness worldwide; the term glaucoma refers to a group of progressive and multifactorial neuropathies associated with cupping and excavation of the optic disc, which induces degeneration of retinal tissue [1]. The most well known risk factor for Primary open-angle glaucoma (POAG) is elevated intraocular pressure (IOP); however, some patients develop glaucoma optic neuropathy in absence of IOP, as other risk factors have been identified like family history of glaucoma, African descent, and older age, use of systemic or topical corticosteroids, among others [2].

Optic disc hemorrhage (ODH) has been linked to the development and progression of primary open-angle glaucoma (POAG). ODH is generally a transient phenomenon that frequently occurs in the supertemporal or inferotemporal area of the optic disc margin correlating with structural and functional changes in glaucomatous eyes.

Despite ODH has been identified as one of the most important risk factors for development and progression of glaucoma, the underlying mechanisms are still not elucidated [2, 3]. Two current theories have been proposed as leading causes of ODH; the mechanical hypothesis establishes that structural changes at the level of the lamina cribosa or the margin of the optic disc or retinal nerve layer turn to lead a mechanical rupture of small blood vessels causing ODH. Moreover, the vascular theory proposes that the pathogenesis of ODH is associated with systemic vascular abnormalities like systemic vascular diseases, platelet dysfunction, primary vascular dysregulation, vasospasm, and dysfunctional regulation of the optic nerve blood flow [3-5].

Prevalence of ODH in glaucoma or suspected glaucoma patients has been estimated in a range between 2 and 33.4%, being higher compared to non-glaucomatous patients in whom a prevalence is estimated between 0-1.4% [6]. Nevertheless, population-based studies have made it possible to determine that the highest prevalence occurs in

eyes with normal pressure glaucoma than elevated IOP and identify other possible underlying related factors like advanced age, aspirin use, diabetes mellitus diagnosis, migraine among others [7].

From September 2014 until January 2019, a cross-sectional study among hypertensive and diabetic patients was conducted in six Colombian cities, aiming to assess the prevalence and the relationships between these two vascular risk factors and glaucoma [8]. We conducted a secondary study willing to assess the relationship between ODH and glaucoma among patients diagnosed with Systemic Hypertension and Diabetes Mellitus.

2. MATERIAL AND METHODS

2.1. DESIGN AND CONTEXT

A cross-sectional study was conducted in six Colombian cities (Bogotá, Buga, Bucaramanga, Cali, Medellín, San Andrés) that included patients over 50 years diagnosed with systemic hypertension and Diabetes Mellitus, patient with associated comorbidities: renal failure, congestive heart failure, sleep apnea, autoimmune diseases, previous intraocular surgery were excluded.

Participants underwent to a complete ophthalmic examination, including IOP measurement by Goldmann tonometry, which was obtained from the average of three values. Gonioscopy was performed in a dark room using a 4-mirror gonio lens (Ocular Instruments Inc., Bellevue, WA) in primary position, with a slit beam less than 2 mm in height, followed by a dilated funduscopy examination with a 78 diopter (D) lens for evaluating the optic disc, (Ocular Instruments Inc., Bellevue, WA). Central corneal thickness (CCT) was calculated based on the average of three consecutive measurements using a PachPen handheld pachymeter (Accutome, iNC., Pennsylvania, USA). Optic nerve examination was conducted with a 78 D lens and pachymetry measurements were obtained.

In suspected cases of glaucoma, the diagnosis was confirmed using visual field (VF) test with the 24-2 Swedish Interactive Threshold Algorithm (Humphrey, Carl Zeiss Meditec, Inc) and optic nerve photos with a DRS camera (digital retinography system, Centervue, Fremont, CA, USA). Glaucomatous eyes had to have at least two consecutive, reliable, and repeatable standard automated perimetry examinations with either a pattern standard deviation (PSD) outside the 95% normal limits or a glaucoma hemifield test result outside normal limits. Reliable visual fields had rates of false positives, fixation losses, and false-negative errors of 20% or less to be

included. Trained glaucoma specialists performed the examinations using standardized protocols.

Suspected and confirmed cases of glaucoma were defined according to the criteria specified by Foster et al. [9]. Established glaucoma was defined as structural and functional evidence of glaucomatous damage in at least one eye that met the following criteria: 1) horizontal or vertical cup-disc ratio > 0.7 , focal glaucomatous disc change (disc hemorrhage, neuroretinal rim notch, marked sloping of rim tissue, a narrowest remaining rim of 0.1 disc diameter or less), cup/disc asymmetry > 0.2 , associated with a glaucomatous Visual Field defect; 2) horizontal or vertical cup-disc ratio > 0.8 , focal glaucomatous disc change, asymmetry > 0.3 with an absence of functional evidence of glaucomatous damage (if the subject could not satisfactorily complete the VF examination). Cases that did not meet all criteria were classified as suspected glaucoma. In addition, VF defects not explained by any other disease, like asymmetry across the horizontal midline, visual defects located in the mid-periphery, or clustered in neighboring test points, were defined as compatible with the disease.

Abdominal Circumference and Body Mass Index. The glaucoma diagnosis was confirmed by structural and functional evidence. Interviews, standardized questionnaires evaluated participants' lifestyles, and other health conditions including socioeconomic status, associated comorbidities, education, and nutrition. The physical examination included measurement of height, weight, abdominal circumference, heart rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Blood Pressure (BP) was measured in a sitting position after 5 minutes of rest using a sphygmomanometer (Welch Allyn, New York, U.S.). The cut-off values of BP were defined according to the guidelines for managing arterial hypertension of the European Society of Hypertension (ESH). BP was measured in a sitting position after 5 minutes of rest using a sphygmomanometer (Welch Allyn, New York, U.S.). The cut-off values of BP were defined according to the 2013 guidelines for managing arterial hypertension of the ESH [10].

This study was conducted according to the Declaration of Helsinki guidelines; the Universidad del Valle, institutional review board reviewed and approved the study protocol (IRB approval number: 030-014). In addition, an informed consent was obtained from all patients that accepted to participate.

2.2. SAMPLE SIZE AND STATISTICAL ANALYSIS

Sample size was estimated considering a precision represented in a relative standard error (Esrel) less than or

Table 1: Sociodemographic, clinical and ocular characteristics of cases with and without primary open-angle glaucoma

Variable	Confirmed (n=142) (%)	Suspected (n=226) (%)	No glaucoma (n=1699) (%)	p value	Total (n=2067) (%)
Age					
50-59	25 (17.61)	73 (32.30)	480 (28.25)	0.001	578 (27.96)
60-69	48 (33.80)	93 (41.15)	664 (39.8)		805 (38.95)
70-79	57 (40.14)	44 (19.47)	445 (26.19)		546 (26.42)
>80	12 (8.45)	16 (7.08)	110 (6.47)		138 (6.68)
Sex					
Female	70 (49.30)	149 (65.04)	1105 (64.05)	0.001	1324 (65.93)
Male	72 (50.70)	77 (34.96)	594 (35.95)		743 (34.07)
Race					
Latin	116 (81.69)	164 (72.57)	1348 (79.34)	0.012	1628 (78.76)
African-Colombian	13 (9.15)	29 (12.83)	118 (6.95)		160 (7.74)
White	13 (9.15)	33 (14.60)	233 (13.71)		279 (13.50)
Marital status					
Other	55 (38.73)	81 (36.00)	7354 (43.23)	0.083	870 (42.13)
Married/Free union	87 (61.27)	144 (64.00)	964 (56.77)		1195 (57.87)
Education level					
High school or less	114 (81.43)	172 (76.79)	1257 (75.22)	0.242	1543 (75.82)
Professional degree	26 (18.57)	52 (23.21)	414 (24.78)		492 (24.18)
Smoker					
Non smoker	79 (56.03)	142 (63.39)	1029 (60.74)	0.593	1250 (60.71)
Former smoker	57 (40.43)	75 (33.48)	593 (35.01)		725 (35.21)
Smoker	5 (3.55)	7 (3.13)	72 (4.25)		84 (4.08)
Systemic diagnosis					
Diabetes mellitus (DM)	14 (9.86)	33 (14.60)	180 (10.60)	0.422	227 (10.99)
Systemic hypertension (SH)	89 (62.68)	129 (57.08)	1013 (59.66)		1231 (59.58)
DM and SH	39 (27.46)	64 (28.32)	505 (29.74)		608 (29.43)
Intraocular pressure					
Mean±standard deviation	15.40±5.03	15.06±4.19	13.93±2.77	0.000	14.15±3.19
Ocular perfusion pressure					
≤40	34 (24.11)	52 (23.42)	221 (13.19)	0.000	307 (15.06)
41-50	63 (44.68)	100 (45.05)	818 (48.81)		981 (48.11)
51-60	31 (21.99)	63 (23.38)	541 (32.28)		635 (31.14)
≥60	13 (9.22)	7 (3.15)	96 (5.73)		116 (5.69)
Mean±standard deviation	45.8±11.75	46.09±7.89	48.05±7.61		47.69±8.03

equal to 2.3%. An expected proportion of the event $p = 50\%$ to maximize the sample size, a reliability level of 95%, a design effect (Deff) of 1 and a population over 50 years of age for Colombia in 2014 equal to 10,672,965 inhabitants (DANE Redatam+SP - ECLAC/CELADE – Estimates based on the 2005 Population Census) were used [11]. For the final sample size calculation, a non-response percentage of 10% was considered. A final sample size of 2,079 was obtained.

Continuous variables were summarized with mean± standard deviation (SD) or median and Interquartile range (IQR), while categorical variables were described with proportions.

The patients were divided into three groups according to the status of diagnosis of Glaucoma: confirmed cases, suspected cases, and those without glaucoma. Binary and categorical characteristics were compared using a chi-square or Fisher's exact tests. A multinomial logistic regression model was applied to determine factors associated with glaucoma. Model selection was performed using a backward selection

methodology and variables with p values <0.20 in bivariate analysis were included. Odds Ratios (OR) were estimated with a 95% confidence interval, and goodness-of-fit was evaluated using a likelihood ratio test and the smallest model deviance. A level of significance of 0.05 was used. All analyses were carried out using Stata13® (STATA Corp, College Station, TX, USA).

3. RESULTS

2085 subjects completed the interview and ophthalmologic examination, of which 18 were excluded because they met one or more exclusion criteria. The average age of the 2067 participants was 65.6 ± 8.8 years; 65.93% (1324) were female, 11.0% (227) had only DM, 59.6% (1231) had only SH, and 29.4% (608) had both diseases. Of 2067 SH and DM patients, 142 were identified with confirmed glaucoma and 226 subjects with suspected glaucoma (Table 1).

3.1. PREVALENCE OF GLAUCOMA

The Prevalence of confirmed POAG was 5.6% [95% CI: 4.6-6.0], with a higher prevalence observed among those with SH only (Table 2).

Table 2: Prevalence of primary open-angle glaucoma

Glaucoma	Total % [95%CI]	Diabetes mellitus (DM) % [95%CI]	Systemic hypertension (SH) % [95%CI]	DM and SH % [95%CI]
Confirmed	5.6 [4.6-6.6]	4.8 [2.4-8.5]	6.2 [4.9-7.7]	4.4 [2.9-6.4]
Suspect	9.1 [7.8-10.4]	11.4 [7.6-16.3]	8.6 [7.1-10.3]	10.5 [8.2-13.2]
Total	14.6 [13.1-16.2]	16.3 [11.7-21.5]	14.9 [12.9-16.9]	13.5 [10.9-16.5]

The proportion of suspected cases was higher among participants with DM. The prevalence of POAG according to age and sex is described in Table 3. Confirmed POAG was more frequent in men of all ages. The prevalence of Optic disc hemorrhage (ODH) was 0.4%, 50% of patients with ODH had a diagnosis of POAG, and 50% of patients with ODH did not have glaucoma.

a response variable), the explanatory variables taken into account were: SH, DM, Retinal Nerve Fiber Layer Defect, smoking, age, sex, ethnicity, BMI, IOP, Central Corneal Thickness, Dyslipidemia, Migraine, Family history of Glaucoma, socioeconomic status, Ocular Perfusion

Pressure, Systolic Perfusion Pressure, Diastolic Perfusion Pressure, Systolic Pressure, Diastolic Pressure, Self Diagnosis of Glaucoma, education level, marital status, occupation, and Abdominal Perimeter. Patients with a diagnosis of SH had an OR of 0.02 (95% CI 0.00 - 0.96); also, patients with Retinal Nerve Fiber Layer Defect presented an OR of 509.40 (95% CI 8.60 - 30152.97) (Table

Table 3: Prevalence of primary open-angle glaucoma according to sex and age

Age	Confirmed primary open-angle glaucoma			Suspected primary open-angle glaucoma		
	Women % [95%CI]	Men % [95%CI]	Total % [95%CI]	Women % [95%CI]	Men % [95%CI]	Total % [95%CI]
50-59	2.7 [1.5-4.9]	6.8 [3.9-11.6]	4.0 [2.7-5.9]	9.5 [7.0-12.8]	11.9 [7.9-17.6]	10.2 [8.0-13.0]
60-69	3.5 [2.2-5.6]	6.0 [3.8-9.4]	4.5 [3.2-6.1]	9.3 [7.0-12.1]	8.4 [5.7-12.1]	8.9 [7.1-11.1]
70-79	6.8 [4.5-10.1]	11.3 [7.7-16.1]	8.6 [6.5-11.3]	7.4 [5.0-10.8]	8.1 [5.2-12.5]	7.7 [5.7-10.2]
>80	5.6 [2.3-12.8]	8.9 [3.3-21.6]	6.7 [3.5-12.4]	10.1 [5.3-18.4]	11.1 [4.6-24.2]	10.4 [6.3-16.9]

5).

3.2. OPTIC DISC HEMORRHAGE AND THE RELATIONSHIP WITH GLAUCOMA

In the multivariate logistic analysis, glaucoma was determined as the response variable. The explanatory variables taken into account were: smoking, age, sex, ethnicity, BMI, Intraocular Pressure (IOP), Central Corneal Thickness, Abdominal Perimeter, Family History of Glaucoma, socioeconomic level, Ocular Perfusion Pressure, Systolic Perfusion Pressure, Diastolic Perfusion Pressure, SH, DM, Systolic Pressure, Diastolic Pressure, optic disc hemorrhage.

Patients from 70 to 79 years of age presented an OR of 2.70 (95% CI 1.49 - 4.88). Women presented an OR of 0.31 (95% CI 0.17 - 0.54). IOP presented an OR of 0.80 (95% CI 0.47 - 1.39). Central Corneal Thickness presented an OR of 0.99 (95% CI 0.98 - 0.99). High Socioeconomic level presented an OR of 0.35 ($p < 0.024$, 95% CI 0.13 - 0.92). Systolic Pressure presented an OR of 1.25 (95% CI 1.13 - 1.39). Optic disc hemorrhage presented an OR of 8.82 (95% CI 1.60 - 48.52) for the presence of Glaucoma (Table 4).

3.3. OPTIC DISC HEMORRHAGE

In multivariate logistic analysis (Optic Disc Hemorrhage as

4. DISCUSSION

Our results found a prevalence of ODH of 0.4%, besides the low prevalence 50% of patients with ODH had a diagnosis of POAG, this is an important risk factor for the presence of glaucoma as RNFL and in our study, ODH presented an OR: 8.82 (95% CI 1.60 - 48.52) for the presence of Glaucoma. Bjerrum first described ODH almost 100 years ago. Since then, ODH has been found to strongly affect the development and progression of Glaucoma [12-14]. ODH is rare, with just a few population-based studies reporting its occurrence. The Beaver Dam Eye Study was a cross-sectional study of 4926 patients. This study found that 0.9 % of patients had ODH [15].

The Blue Mountains Eye Study reported an overall prevalence of ODH in either or both eyes of 1.4%. ODH increased with age (OR 2.2 per decade; CI, 1.7-2.8 per decade and was higher in women (OR 1.9; CI, 1.0-3.5. The overall prevalence in subjects with open-angle glaucoma was 13.8% (8% in high-pressure glaucoma and 25% in low-pressure glaucoma). Disc hemorrhages were associated with increased intraocular pressure (OR, 1.7 per 5 mmHg; CI,

Table 4: Optic nerve hemorrhage and the relationship with glaucoma

Variable	Glaucoma			Glaucoma suspected		
	Coef (RRR)	[95% CI]	Sig.	Coef (RRR)	[95% CI]	Sig.
Smoking status						
Non smoker	1	-		1	-	
Former smoker	1.169	0.746-1.832	-	1.01	0.706-1.445	-
Smoker	0.893	0.299-2.668	-	0.778	0.318-1.906	-
Age						
50-59	1	-	-	1	-	-
60-69	1.236	0.684-2.233	**	0.944	0.645-1.383	-
70-79	2.646	1.464-4.783	*	0.574	0.349-0.944	**
>80	1.609	0.613-4.224	-	1.053	0.518-2.142	-
Sex						
Male	1	-	-	1	-	-
Female	0.379	0.239-0.602	**	0.978	0.663-1.442	-
Ethnicity						
Latino, mestizo, non white	1	-	-	1	-	-
African-Colombian	1.06	0.515-2.182	-	1.807	1.07-3.052	**
White	0.641	0.306-1.346	-	1.344	0.85-2.124	-
Body Mass Index						
Normal	1	-	-	1	-	-
Overweight	0.78	0.456-1.335	-	1.126	0.73-1.739	-
Obesity	0.848	0.452-1.592	-	1.224	0.733-2.041	-
Intraocular pressure (mmHg)	0.803	0.685-0.941	**	0.828	0.717-0.956	**
Corneal Central Thickness (microns)	0.991	0.985-0.997	**	0.995	0.99-1	**
Abdominal perimeter						
Low risk	1	-	-	1	-	-
Increased risk	0.978	0.491-1.948	-	0.935	0.557-1.569	-
High risk	1.206	0.622-2.336	-	0.624	0.372-1.045	*
Family history of glaucoma						
No	1	-	-	1	-	-
Yes	2.11	1.333-3.342	**	1.013	0.683-1.502	-
Socioeconomic level						
Level 1	1	-	-	1	-	-
Level 2	0.559	0.29-1.076	*	1.083	0.633-1.853	-
Level 3	0.605	0.321-1.141	-	0.82	0.474-1.418	-
Level 4	0.513	0.236-1.115	*	0.847	0.446-1.609	-
Level 5	0.353	0.133-0.938	**	0.839	0.379-1.861	-
Level 6	0.197	0.022-1.737	-	1.42	0.426-4.731	-
Ocular perfusion pressure	0.962	0.91-1.016	-	0.966	0.924-1.01	-
Diastolic perfusion pressure	0.733	0.627-0.857	**	0.776	0.673-0.895	***
Systolic perfusion pressure	1	-	-	1	-	-
Systemic hypertension						
No	1	-	-	1	-	-
Yes	1.372	0.609-3.089	-	0.634	0.78-1.062	*
Diabetes mellitus						
No	1	-	-	1	-	-
Yes	0.879	0.55-1.391	-	1.116	0.768-1.624	-
Systolic blood pressure	1.253	1.134-1.385	**	1.191	1.086-1.305	***
Diastolic blood pressure	1	-	-	1	-	-
Optic nerve hemorrhage						
No	1	-	-	1	-	-
Yes	8.723	1.616-47.073	-	1.974	0.206-18.934	-
Constant	1.646	0.04-66.918	-	3.583	0.184-69.882	-

*** $p < 0.01$; ** $p < 0.05$; * $p < 0.1$.

1.3-2.3 per 5 mmHg), pseudoexfoliation (OR, 3.5; CI, 1.1-11.8), diabetes (OR, 2.9; CI, 1.4 - 6.3), and increased systolic blood pressure (OR, 1.1 per 10 mmHg; CI, 1.0 - 1.3) after adjusting for age and gender [16]. Moreover, the Bridlington Eye Assessment Project (BEAP) was a cross-sectional study of 3549 participants' ≥ 65 years performed between 2002 and 2006. The overall prevalence of ODH was 1.49%, increasing from 1.17% (65- to 69-year age group) to 2.19% (80- to 84-year age group), $p = 0.06$. DH

was associated with increasing age (OR 1.05, 95% CI 1.001-1.10, $p = 0.03$) and glaucoma (OR 10.2, 95% CI 5.32 - 19.72) [7].

In our study, 50 % of patients with ONH had glaucoma, and 50% of patients with ONH did not have glaucoma. The Blue Mountains eye study showed similar results. 27.5 % of patients with POAG presented ONH, compared to 72.5% of normal patients. Among subjects without open-angle glaucoma, disc hemorrhages were more frequent in eyes

with larger vertical cup-disc ratios and subjects with a history of migraine headaches (OR, 2.2; CI, 1.1 - 4.6).

Within the two purposed theories about the pathophysiology of ODH, the ODH vascular hypothesis has suggested that

Table 5: Optic disc hemorrhage logistic regression

Optic disc hemorrhage	OR	[95% CI]	Sig.
Systemic hypertension			
No	1	-	-
Yes	0.19	0-0.962	**
Diabetes mellitus			
No	1	-	-
Yes	0.108	0.006-1.817	-
Retinal nerve fiber layer effect			
No	1	-	-
Yes	509.397	8.606-30152.971	***
Smoking status			
Non smoker	1	-	-
Former smoker	0.163	0.01-2.594	-
Smoker	1	-	-
Age			
50-59	1	-	-
60-69	1	-	-
70-79	4.019	0.259-62.164	-
>80	3.489	0.049-247.526	-
Ethnicity			
Latino, mestizo, non white	1	-	-
African-Colombian	3.564	0.307-41.343	-
White	1	-	-
Body Mass Index			
Normal	1	-	-
Overweight	0.155	0.011-2.15	-
Obesity	0.262	0.019-3.544	-
Intraocular pressure (mmHg)	1.915	0.601-6.069	-
Corneal Central Thickness (microns)	1.001	0.966-1.033	-
Dyslipidemia			
No	1	-	-
Yes	10.265	0.901-116.975	*
Migraine			
No	1	-	-
Yes	0.581	0.028-22.577	-
Family history of glaucoma			
No	1	-	-
Yes	0.581	0.049-6.923	-
Socioeconomic level			
Level 1	1	-	-
Level 2	0.645	0.04-10.399	-
Level 3	0.156	0.004-6.447	-
Level 4	1	-	-
Level 5	0.027	0-9.124	-
Level 6	1	-	-
Ocular perfusion pressure	1.071	0.847-1.353	-
Systolic perfusion pressure	1.749	0.524-5.839	-
Diastolic perfusion pressure	1	-	-
Systolic blood pressure	0.698	0.318-1.534	-
Diastolic blood pressure	1	-	-
Awareness of glaucoma			
No	1	-	-
Yes	1.036	0.018-59.437	-
Educational level			
High school	1	-	-
Professional degree	1.669	0.11-25.174	-
Marital status			
Free union	1	-	-
Married	0.303	0.034-2.655	-
Occupational status			
Retired	1	-	-
Independent/employee	2.144	0.034-2.655	-
Home duties	0.17	-	-
Abdominal perimeter			
Low risk	1	-	-
Increased risk	1.521	0.107-21.678	-
High risk	1	-	-
Constant	0	0-17929.22	-

*** $p < 0.01$; ** $p < 0.05$; * $p < 0.1$.

systemic vascular abnormalities induce micro- occlusion of small retinal vessels, damage the vessels located around the optic nerve head or produce damage to vessel walls contributing to the establishment of this condition [3]. Hypertension, Diabetes Mellitus, and atherosclerosis are conditions that induce ischemia around the optic nerve, increasing the probability of developing ODH, as in the patients with primary vascular dysregulation; autoregulation of ocular blood flow is impaired because of increased retinal-vessel stiffness [3, 17]. Furlanetto et. al conducted a study cohort study where their results were consistent with previous studies where hypertension was a significant risk factor for ODH and other systemic comorbidities like migraine, Raynaud phenomenon, diabetes mellitus and the use of systemic medication for diabetes and hypertension like B-blockers and antidiabetic agents [17].

Within the limitations of our study, although our demonstrations that the presence of ODH is associated with the presence of glaucoma. We cannot establish a causal relationship. In the same way, our confidence intervals are wide compromising the accuracy of the estimate and there are no other studies to our known conducted in the Colombian population. However, our study is the first study conducted in the Colombian population addressed to elucidate a relationship between ODH and the presence of glaucoma in Colombian adults older than 50 years diagnosed with systemic hypertension and diabetes mellitus. In our opinion, this study lay the foundations to explore this condition and in the future seek to establish related associations due to the burden of disease that it represents worldwide and particularly for low- and middle-income countries such as Colombia [18]. In our country, cardiovascular diseases are a public health problem, being as well the first cause of mortality [19].

5. CONCLUSIONS

Besides the prevalence of glaucoma in our study was low, the association between ODH and glaucoma has been extensively studied in recent decades, and multiple factors associated with the triggering of ODH, have been identified. This study supports the conduction of other studies as well as the development of public policies to strengthen primary care in comprehensive ophthalmological care.

6. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial

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8. REFERENCES

1. Kang JM, Tanna AP. Glaucoma. *Med Clin North Am.* 2021;105(3):493-510. doi: 10.1016/j.mcna.2021.01.004.
2. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA.* 2014;311(18):1901-11. doi: 10.1001/jama.2014.3192.
3. Kim KE, Park KH. Optic disc hemorrhage in glaucoma: pathophysiology and prognostic significance. *Curr Opin Ophthalmol.* 2017;28(2):105-12. doi: 10.1097/ICU.0000000000000345.
4. Kurvinen L, Harju M, Saari J, Vesti E. Altered temporal peripapillary retinal flow in patients with disc hemorrhages. *Graefes Arch Clin Exp Ophthalmol.* 2010;248(12):1771-5. doi: 10.1007/s00417-010-1441-7.
5. Patel HY, Buys YM, Trope GE. Nailfold capillaroscopy assessment in patients with glaucoma with a current optic disc hemorrhage. *Can J Ophthalmol.* 2015;50(2):155-8. doi: 10.1016/j.cjco.2014.11.013.
6. Suh MH, Park KH. Pathogenesis and clinical implications of optic disc hemorrhage in glaucoma. *Surv Ophthalmol.* 2014;59(1):19-29. doi: 10.1016/j.survophthal.2013.03.005.
7. Wilde C, Poostchi A, Narendran R, MacNab HK, Hillman JG, Alexander P, et al. Prevalence of optic disc haemorrhages in an elderly UK Caucasian population and possible association with reticular pseudodrusen-the Bridlington Eye Assessment Project (BEAP): a cross-sectional study (2002-2006). *Eye (Lond).* 2019;33(4):580-6. doi: 10.1038/s41433-018-0263-4.
8. Rivera CE, Cantor E, Castillo A, Martinez A, Newball L, Rueda JC, et al. Prevalence of Primary Open Angle Glaucoma among Patients with Diagnosis of Systemic Hypertension and Diabetes Mellitus: The Colombian Glaucoma Study. *Open J Ophthalmol.* 2020;10(02):99-114. doi: 10.4236/ojoph.2020.102012.
9. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J.* 2013;34(28):2159-219. doi: 10.1093/eurheartj/ehi151.
10. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol.* 2002;86(2):238-42. doi: 10.1136/bjo.86.2.238.
11. Colombian Government. Census 2005. Available from: <https://www.dane.gov.co/index.php/en/statistics-by-topic-1/population-and-demography/census-2005> (accessed August 2022).
12. Ishida K, Yamamoto T, Sugiyama K, Kitazawa Y. Disk hemorrhage is a significantly negative prognostic factor in normal-tension glaucoma. *Am J Ophthalmol.* 2000;129(6):707-14. doi: 10.1016/s0002-9394(00)00441-4.
13. De Moraes CG, Prata TS, Liebmann CA, Tello C, Ritch R, Liebmann JM. Spatially consistent, localized visual field loss before and after disc

hemorrhage. *Invest Ophthalmol Vis Sci.* 2009;50(10):4727-33. doi: 10.1167/iov.09-3446.

14. Ernest PJ, Schouten JS, Beckers HJ, Hendrikse F, Prins MH, Webers CA. An evidence-based review of prognostic factors for glaucomatous visual field progression. *Ophthalmology.* 2013;120(3):512-9. doi: 10.1016/j.ophtha.2012.09.005.

15. Klein R, Klein BE, Linton KL, De Mets DL. The Beaver Dam Eye Study: visual acuity. *Ophthalmology.* 1991;98(8):1310-5. doi: 10.1016/s0161-6420(91)32137-7.

16. Ong LS, Mitchell P, Healey PR, Cumming RG. Asymmetry in optic disc parameters: the Blue Mountains Eye Study. *Invest Ophthalmol Vis Sci.* 1999;40(5):849-57.

17. Furlanetto RL, De Moraes CG, Teng CC, Liebmann JM, Greenfield DS, Gardiner SK, et al. Risk factors for optic disc hemorrhage in the low-pressure

glaucoma treatment study. *Am J Ophthalmol.* 2014;157(5):945-52. doi: 10.1016/j.ajo.2014.02.009.

18. World Health Organization (WHO). WHO launches first World report on vision. Available from: <https://www.who.int/es/news/item/08-10-2019-who-launches-first-world-report-on-vision> (accessed August 2022).

19. Ministry of Health and Social Protection Directorate of Epidemiology and Demography. Mortality in Colombia period 2020-2021. Available from: <https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/GC/Fl/mortalidad-colombia-periodo-2020-2021.pdf> (accessed August 2022).